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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,104	08/02/2005	Mark Ibberson	ARS-107	9640

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EXAMINER	
STOICA, ELLY GERALD	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
10/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,104	IBBERSON ET AL.	
	Examiner	Art Unit	
	Elly-Gerald Stoica	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-91* is/are pending in the application.

4a) Of the above claim(s) *64-86 and 88-91* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-63 and 87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/23/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I claims 58 (in part), 59-63 and 87 as drawn to a polypeptide of Seq. Id. No.: 2, in the reply filed on 09/20/2007 is acknowledged. The traversal is on the ground that the invention does not lack unity because the DNA, the polypeptide and primers are connected as a special technical feature. This is not found persuasive because they do not present a common structure linked to a common function.

The requirement is still deemed proper and is therefore made FINAL.

Status of the claims

2. Claims 58-91 are pending. Claims 64-86, 88-91 are withdrawn from prosecution as non-elected claims. Claims 58 (in part), 59-63 and 87, as drawn to the polypeptide of Seq. Id. No.: 2 are subject to examination.

Claim Objections

3. Claim 58 is objected to for encompassing non-elected inventions.

4. Claim 87 is objected to because of the following informalities: in line 1, polypeptide**s** should read polypeptide and comprise should read comprises. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 58, 59-63 and 87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to an isolated polypeptide having Seq. Id. No.: 2 or an active variant of it wherein any amino acid specified in the chosen sequence is non-conservatively substituted, provided that no more than 15% of the amino acid residues in the sequence are so changed and said active variant retains chemotactic activity. Also claimed is a polypeptide encoded by a nucleic acid of 30 nucleotides having 85%

identity to the nucleic acid encoding the polypeptide of Seq. Id. No.: 2. The polypeptide further comprises a cytotoxic agent.

The specification teaches that methods were used to detect the open reading frame (ORF) for a putative protein that might have chemotactic activity (p.33, line 13 to p. 34, line 14) and the methods of isolating that DNA sequence. However, the instant specification does not teach any functional characteristics of the peptide encoded by Seq. Id. No.: 2, apart from the assertion of the Applicant that it might have chemotactic activity. The specification teaches the polypeptide of the Seq. Id. No.: 2 and the fact that it has less than 30 % homology with known proteins in the protein databases (p. 33, lines 21-23) underscores the novelty of the peptide. However, the specification does not teach any variant, fragment, or derivative of the peptide. The requirement that the peptide retain chemotactic activity, without specifying what the region of the peptide is necessary to be preserved, adds to the unpredictability of obtaining and using an untested novel protein. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with the polypeptide of Seq. Id. No.: 2. Absent from the specification is any indication of the nature of the chemotactic activity of the protein or the conditions under which this putative activity is exerted.

The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's

sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions as long they are within the 15% of the number of residues. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1): 34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics

12:425-427). Moreover, the specification recites a series of methods known in the art that could be used for assessing the claimed activity but such protocols are merely an invitation to experiment to determine if the variant claimed have chemotactic activity. Regarding the cytotoxic agent comprised by the polypeptides, since one does not know which particular activity is encompassed by the protein, it would require undue experimentation to choose an appropriate cytotoxic reagent for a novel and untested protein.

Due to the large quantity of experimentation necessary to generate the great number of derivatives recited in the claims and possibly screen the same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function as well as the unpredictability of a novel protein to posses the activity claimed based just on the primary structure; undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

7. Claims 58, 59-63 and 87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The specification discloses the structure of a peptide having Seq. Id. No.: 2 that might possess chemotactic activity without underscoring the structural feature to be conserved. It does not identify any particular amino acids amenable to non-conservative substitution in order to maintain the claimed activity. The specification also defines the polypeptide as being encoded by a DNA sequence that exhibits 85% identity over a stretch of 30 nucleotides with a nucleic acid that code for the protein of Seq. Id. No. 2. Accordingly, the claimed polypeptide could be encoded any 8-9 amino acid stretch of the polypeptide of Seq. Id. No. 2. without any requirement for activity related to this particular structure. This, again, does not constitute an adequate written description for a polypeptide, let alone a genus of polypeptides having any activity linked to them. In the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus of peptides that are active fragments, derivatized peptides or antigenic fragments recited in the claim.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

'written description' inquiry, whatever is now claimed" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See Vas-Cath at page 1116).

Therefore, only the peptide consisting of the sequence of Seq. Id. No.: 2 or chemotactic fragments thereof, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 58, 59-63 and 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For claim 58 part e), it is not clear how the recitation would include or exclude any additional embodiments.

For claim 58 part f), it is unclear how a protein that has inadequate written description (see supra) would define a product that binds to it, since a person of ordinary skill in the art would not be able to know what the "binding protein" would bind to.

For claim 58 part i) it is unclear what the meets and bounds of the term "high stringency" are.

For claim 62 is unclear if by "active variant" is meant chemotactic and also unclear is what is meant by "chosen sequence". This aspect is indefinite especially since the claim 63 recites "active variant or derivatized polypeptide" and then requires chemotactic activity.

Therefore, the meets and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 58, 59-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bates, K. et al. (Database EMBL 'Online! HTG, March 7,2000, Accession No. AL159154, XP-002231616, "Human DNA sequence from clone RP11-428623 on chromosome 13"-document R5 cited by the Applicants in the IDS filed 01/23/2006), in view of Sibson et al. (WO/94/01548).

Bates et al. disclose the DNA sequence of the human chromosome 13. One of the Open reading frames is the open reading frame that codes for the peptide of the instant Application. An alignment of the reverse strand of the sequence that codes for the peptide of Seq. Id. No.: 2 to the partial sequence of chromosome 13 taught by Bates et al. presented below, clearly shows the presence of the sequence between the positions 66474-66776.

NCBI **Blast 2 Sequences results**

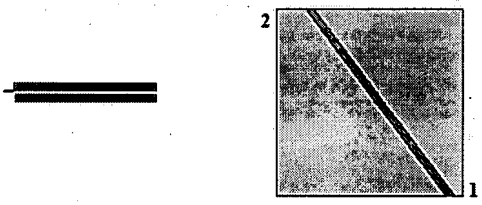
PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2
x_dropoff: 0 expect: 10.0000 wordsize: 11 Filter ☐ View option Standard
Masking character option X for protein, n for nucleotide Masking color option Black
☐ Show CDS translation Align

Sequence 1: gi|13157532|Human DNA sequence from clone RP11-428G23 on chromosome 13 Contains part of a novel gene (KIAA0916), complete sequence
Length = 401 (66400 .. 66800)

Sequence 2: lcl|65536
Length = 303 (1 .. 303)



NOTE:Bitscore and expect value are calculated based on the size of the nr database.

NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

```
 Score =  583 bits (303),  Expect = 2e-163
 Identities = 303/303 (100%), Gaps = 0/303 (0%)
 Strand=Plus/Minus

Query  66474  CTACCAACCTGTACAGCATGCTGGTGTACTGAATACTGTAGGCAACTGTAACCCATTAGT  66533
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  303    CTACCAACCTGTACAGCATGCTGGTGTACTGAATACTGTAGGCAACTGTAACCCATTAGT  244

Query  66534  AAGTATTTCTGCATGTAAACATAGAAAAGTTATAGTCAAAGTACTTATTATAATCTTATG  66593
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  243    AAGTATTTCTGCATGTAAACATAGAAAAGTTATAGTCAAAGTACTTATTATAATCTTATG  184

Query  66594  GGAACACCTTAGCATACGCAGTCCATCACTGACCAAAATACTGTTATACAGTGCATAACT  66653
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  183    GGAACACCTTAGCATACGCAGTCCATCACTGACCAAAATACTGTTATACAGTGCATAACT  124

Query  66654  GTGTATACACATACATACATATATAGGTATATATATATAAAATAGTGTGTCTGCATGCTT  66713
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  123    GTGTATACACATACATACATATATAGGTATATATATATAAAATAGTGTGTCTGCATGCTT  64

Query  66714  ATATATCTTCACAAGAAGAAACACAAGAAGAATAAACTGTAAAACAATGACATTCATTAC  66773
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  63     ATATATCTTCACAAGAAGAAACACAAGAAGAATAAACTGTAAAACAATGACATTCATTAC  4

Query  66774  CTC  66776
              |||
Sbjct  3      CTC  1


CPU time:      0.10 user secs.       0.04 sys. secs          0.14 total secs.
```

Therefore, the sequence was known as an ORF as proved by alignment and was part of a novel gene, KIAA0916. Bates et al. are silent about using the sequence to obtain a peptide labeled or not.

Sibson et al. disclose that it is generally useful to place a desired DNA sequence into an expression vector, host cell, and express the encoded protein, as well as to raise antibodies to protein encoded by such DNA. See pages 8-13.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the DNA disclosed by Bates et al. to express and then isolate the encoded polypeptide as taught by Sibson et al., in view of Sibson et al.'s suggestion that it would be desirable to do so, as cited above.

Claim 87 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bates, K. et al. (Database EMBL 'Online! HTG, March 7,2000, Accession No. AL159154, XP-002231616, "Human DNA sequence from clone RP11-428623 on chromosome 13"-document R5 cited by the Applicants in the IDS filed 01/23/2006), in view of Sibson et al. (WO/94/01548) and in further view of Scherberg N.H. (U.S. Pat. No. 4,383,033).

The considerations of Bates et al. and Sibson et al. were presented supra. They do not expressly teach labeling the proteins obtained.

Scherberg teaches radiolabeled proteins which may be employed advantageously in diagnosis to provide marker compounds for chromatographic detection, immunoprecipitation, and serum clearance testing (abstract and col. 4, lines 20-25).

It would have been obvious for a person of ordinary skill in the art to label the proteins, obtained according to the teachings of Bates et al., Sibson et al., and as taught by Scherberg with a reasonable expectation of success. The motivation to do so was offered by Scherberg by the teaching of the usefulness of labeled proteins.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elly-Gerald Stoica whose telephone number is (571) 272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER